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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/816,653	03/23/2001	Diane Pennica	10716-57/CURA233/GN1885R1	6857

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/14/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/816,653	PENNICA ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,32 and 35-48* is/are pending in the application.

4a) Of the above claim(s) *32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3 and 35-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Response to Amendment

The Amendment filed August 18, 2003 (Paper No. 19) in response to the Office Action of March 17, 2003 is acknowledged and has been entered.

It is noted that claim 32 was omitted from the originally filed claims. The docket team has renumbered the claims in accordance with 37 CFR 1.126. Claims 33-35 were renumbered as Claims 32-34. Newly submitted claims 36-49 were renumbered as Claims 35-48.

Claims 2, 4-31, and 33-34 were cancelled.

Claim 32, drawn to a method of screening a sample of hSTRA6 gene mutations, has been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claims 1, 3, and 35-48 are under consideration. (Dependencies within Claims 35-48 have also been renumbered accordingly. For example, Claim 38, now reads the polypeptide of claim ~~36~~ 35, wherein said amino acid sequence has at least 98% sequence identity to a sequence of SEQ ID NO:4.)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Rejections Maintained:

It is noted that applicant's have combined their arguments in addressing the rejections under 35 USC 101, and 112, 1st paragraph (enablement). Hence, the response below also combines the rejections under 35 USC 101, and 112, 1st paragraph (enablement).

Claims 1 and 3 remain rejected, and new claims 35-48 are rejected under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph (enablement), because the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons of record in Paper No. 17, pages 3-6.

Applicants argue (Paper No. 16, pages 5-7) that they have identified a new human STRA6-like polypeptide that is a downstream target in the Wnt-1 oncogene signaling pathway. Applicants further contend that this polypeptide exhibits strong homologies and sequence identity to the mSTRA6 protein and that they also share structural and cell biological features. Based on these features, applicants argue that utilities for hSTRA6-like polypeptide include its use as a diagnostic marker for cancers such as colon and breast cancer and melanoma and its use in the treatment of said cancers. Applicants argue that the utility is credible because mouse (mSTRA6) is differentially expressed in Wnt-1 transformed cells, indicating that human (hSTRA6) is a target in the Wnt-1 signaling pathway and which, when perturbed, results in oncogensis. Applicants further submit that references made available after the filing date of the instant application (i.e. Szeto *et al.*, 2001; Tice *et al.* 2002) support the assertion that STRA6 plays an important role in cancers driven by Wnt-1. These arguments have been carefully considered but are not found persuasive.

The Office has previously considered the sequence similarity between the STRA6-like polypeptide and mSTRA6 protein, and, based on the state of the art, concluded that evidence

based on protein sequence homology does not alone permit extrapolation to an isolated amino acid's biological function or use thereof. Thus, applicants' assertions that the STRA6-like polypeptide shares biological features of mSTRA6, including its possible role as a downstream target in the Wnt-1 oncogene signaling pathway, are insufficient to obviate the rejections. Furthermore, with regards to the post-filling date references, the state of the art that exists at the *filing* date of the application is used to determine whether a particular disclosure is enabling as of the filing date. Publications dated after the filing date providing information publicly first disclosed after the filing date generally cannot be used to show what was known at the time of filing. MPEP 2164.05(a); In re Gunn, 537 F.2d 1123, 1128, 190 USPQ 402,405-06 (CCPA 1976); In re Budnick, 537 F.2d 535, 538, 190 USPQ 422, 424 (CCPA 1976). Hence, arguments presenting the role of STRA6 (a molecule which applicants assert is substantially identical to the presently claimed STRA6-like polypeptide) via Szeto *et al.* (2001) and Tice *et al.* (2002) on page 7 of Paper No. 19 have not been considered.

Applicants further argue (Paper No. 19, page 7) that STRA6-like polypeptide will likely have the same utilities as the aforementioned STRA6 because STRA6-like polypeptide exhibits similar upregulation (10.9-fold (Quantitative PCR), 11-fold (Quantitative Expression Analysis)) as STRA6. This argument has been considered but is not found persuasive for the reasons set forth above. Further, those of skill in the art recognize that expression of mRNA, specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression. For example, Fu *et al.* (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53

gene. Furthermore, Rama *et al.* (Biochem. J. Vol. 318, 1996, pages 333-341) teach that the glucocorticoid, betamethasone, increased mRNA expression of cholinephosphate cytidylyltransferase (CT) as determined by RT-PCR and Southern analysis, but did not alter the levels of the CT enzyme as assayed by Western blotting (abstract, and page 339, 2nd column, 2nd paragraph). In fact, it is well documented that the basic molecular biology of eukaryotic gene transcription is tightly regulated. Alberts *et al.* (Molecular Biology of the Cell, 3rd edition, 1994, page 465) teach that translation of ferritin mRNA into ferritin polypeptide is blocked during periods of iron starvation. Likewise, if excess iron is available, the transferrin receptor mRNA is degraded and no transferin receptor polypeptide is translated. Hence, the predictability of protein translation and its possible utility as a diagnostic are not necessarily contingent on the levels of mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Likewise, the claims are drawn to STRA6-like polypeptides, variants, and fusions thereof and there is no evidence to suggest that the differential expression patterns observed on page 82 of the disclosure would provide a diagnostic and or therapeutic utility for the claimed invention. If molecules such as STRA6-like polypeptides are to be used as a surrogate for a disease state, some disease state must be identified in some way with the molecules. There must be some expression pattern that would allow the claimed polypeptides to be used in a diagnostic/therapeutic manner. Therefore, one needs to know, e.g., that the claimed polypeptide is present only in cancer tissue to the exclusion of normal tissue. Thus, in the absence of any correlation between the claimed STRA6 polypeptide with any known disease or disorder, any information obtained from various expression profiles in both normal and

transformed cells only serves as the basis for further research on the observation itself. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Claim 1 remains rejected, and new claims 35-37, and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record in Paper No. 17, page 6-8.

Applicants argue (Paper No. 19, bottom of page 7, and pages 8-9) that they were in full possession of the claimed invention at the time of filing because the sequences of the polypeptides are given in the specification and useful variants are described. Applicants argue that compliance with the written description does not require an applicant to describe exactly the subject matter claimed; rather the description must allow one of ordinary skill in the art to recognize that the applicant has invented what is claimed. Applicants argue that they have provided an adequate description of the claimed invention in the form of SEQ ID NO:2 and 4. Applicants submit that well-known principles guide those of skill in the art to produce functional variants. Applicants further point to the teachings of Bowie *et al.* (1990) to validate their argument that variant STRA6 sequences can be made consistent with the teachings of the specification. These arguments have been carefully considered but are not found persuasive. The claims are drawn to polypeptides having at least 80%, 90%, 98% or 99% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed

distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity. And, the fact that it would require further experimentation to those of skill in the art in order to produce the multitude of variant polypeptides as claimed does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Factors to be considered when determining whether or not the claimed invention meets the written description guidelines generally include the disclosure of complete or partial structures, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

New Rejections:

Claims 44 and 46 are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. These are new matter rejections.

Claim 44 is drawn to the polypeptide of Claim 43, comprising the amino acid sequence of SEQ ID NOs: 2 *and* 4. Applicants point out (Paper No. 19, page 4) that support for the claim can be found on page 35, lines 14-17. However, the specification on page 35 only supports one particular *species* of a polypeptide that comprises SEQ ID NO:2 and 4 in the form of a fusion

protein that *includes* the "internal fragment from mouse STRA6 (comprised in SEQ ID NO:7)". Hence, the limitation of a particular species as disclosed in the specification does not provide support for the newly added genus claim drawn to a polypeptide comprising the amino acid sequence of SEQ ID NOs: 2 *and* 4. Thus, this is a new matter rejection.

Claim 46 is drawn is drawn to the polypeptide of Claim 45, wherein the fusion protein comprises various polypeptides including human growth hormone, green fluorescent protein, red fluorescent protein, yellow fluorescent protein, blue fluorescent protein, luciferase, etc. Applicants point out (Paper No. 19, page 4) that support for the claim can be found in page 35 and in Table C (page 36). It is noted, however, that there is no support for "yellow fluorescent protein" on these pages. Thus, this is a new matter rejection. Additionally, it is assumed for examination purposes that recitation of "RFP" and "BFP" in Table C refer to red fluorescent protein and blue fluorescent protein, respectively. If this is an incorrect assumption, then it should also be noted that there is no support for red fluorescent protein and blue fluorescent protein.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by any one of the following:

(1) Pennica *et al.* US Patent Application No: 20020156252A1, Prior Filing Date: 01-13-2000.

(2) Pennica *et al.* US Patent Application No: 20020173461A1, Prior Filing Date: 01-13-2000.

(3) Baker *et al.* US Patent Application No: 20030149239A1, Prior Filing Dates: 1997, 1998.

(4) Baker *et al.* US Patent Application No: 20030187201A1, Prior Filing Dates: 1997, 1998, 1999.

(5) Baker *et al.* US Patent Application No: 20030187202A1, Prior Filing Dates: 1997, 1998.

(6) Baker *et al.* US Patent Application No: 20030187203A1, Prior Filing Dates: 1997, 1998.

The newly amended claim is drawn to an isolated polypeptide comprising an amino acid sequence having at least **99%** sequence identity to a sequence of SEQ ID NO:2. Each of the above references (also see attached sequence comparisons at the end of this action) teach an isolated polypeptide comprising an amino acid sequence having at least 99% sequence identity to SEQ ID NO:2.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection/objection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol Ph.D.
Examiner
Art Unit 1642

GBN